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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/442,111	11/17/1999	SHAWN DEFREES	14137-01382O	5434

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/442,111	DEFREES ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53,55-58 and 60-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53,55-58 and 60-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The finality of the previous Office Action has been withdrawn in view of new rejections and new grounds of rejection.

2. Claims 53, 55-58, and 60-74 are pending and under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 53, 55-58, and 60-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed 04/04/2005 have been fully considered but are not persuasive. Applicants' position is that the novelty of the claimed methods is in the method steps and that accessory enzymes, glycosyltransferases, and product saccharides are adequately described in the specification. The Examiner respectfully disagrees for reasons of record as stated below.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001,which states:

> "*Eli Lilly* explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of compounds is claimed. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can

> do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed." (see p. 1100, 1st column, line 47 to 2nd column, line 2).

Genus claims 53, 55-58, and 60-74 encompass a genus of accessory enzymes, a genus of glycosyltransferases, and a genus of product saccharides, where the scope of the each genus includes many members from many biological sources with differing amino acid sequences and structures, and many product saccharides differing in structural, chemical, and physical characteristics.

Example 18 in the USPTO Synopsis of Application of Written Description Guidelines differs from the claims in that there is substantial variation between members of each claimed genus of accessory enzymes, a genus of glycosyltransferases, and a genus of product saccharides. Thus, the conclusion that since Example 18 meets the written description requirement then the instant invention meets the written description requirement does not apply to the instant claims.

The recitation of the names of the chemical compounds of each genus (e.g., accessory enzyme and glycosyltransferase) does not define any structural features commonly possessed by each claimed genus nor define any structural features commonly possessed by each claimed genus. Furthermore, the specification does not describe and define any structural features commonly possessed by each claimed genus.

The described transformed *E. coli* expressing a CMP-sialic acid synthetase/alpha 2,3-sialyltransferase fusion protein is used in the production of 3'-sialyllactose is not adequate to describe the full scope of the genus claims since the accessory enzymes and glycosyltransferases of the genus are expected to vary in amino acid sequence and structure, and there is no disclosure of a significant structural or functional element or property common to all members of the genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of

the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of these considerations, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed genus of accessory enzymes, a genus of glycosyltransferases, and a genus of product saccharides.

Claim Rejections - 35 U.S.C. § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 53, 56-58, 60, 65-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Samain et al. (Carbohydr Res. 1997 Jul 11;302(1-2):35-42; PTO 1449 filed 3/24/2003) in view of Ullrich et al. (J Bacteriol. 1995 Dec;177(23):6902-9).

The teachings of Samain et al. have been stated in the Office Action dated 02/20/04 and are reproduced here. Samain et al. teach a method for making penta-N-acetyl-chitopentaose (2.5g/L) by culturing a *E.coli* transformed with heterologous genes, specifically, expressing *nodC* or *nodBC* genes (see Abstract and entire publication). Samain et al teach that UDP-N-acetylglucosamine is the sugar donor for synthesis of N-acetylated chitooligosaccharide by NodC (see "(4)", left column, p. 36). The taught NodC (chitin oligosaccharide synthase E.C. 2.4.1.16) "consists essentially" of a catalytic domain of a glycosyltransferase. Samain et al teach that the said *E.coli* cells were cultured and disrupted by boiling and the produced chitooligosaccharides were purified by charcoal adsorption and ion-exchange chromatography.

The teachings of Samain et al. differ from the claims in that transformed *E.coli* does not have a heterologous accessory enzyme for forming a nucleotide sugar.

Ullrich et al. teach the *glmU* gene from gonococcus strain MS11 which encodes N-acetylglucosamine 1-phosphate uridyltransferase involved in the synthesis of UDP-GlcNAc, which is a key nucleotide sugar metabolite in the synthesis of lipopolysaccharide, peptidoglycan, and sialic acids. Ullrich et al. further teach that this *glmU* gene from gonococcus strain MS11 was successfully transformed in to *E.coli* host cells (see entire publication, especially **RESULTS** section pp. 6903-6908).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Samain et al. such that the transformed *E.coli* taught by Samain et al. is transformed with the *glmU* gene encoding N-acetylglucosamine 1-phosphate uridyltransferase taught by Ullrich et al. One of ordinary skill in the art at the time the invention was made would detect and isolate the product saccharide for the purposes of quantifying and determining the purity of the product saccharide.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of having an *E.coli* host cells that can overproduce UDP-GlcNAc which in turn can be used in the method of Samain et al. for making penta-N-acetyl-chitopentaose. Furthermore, it is within the purview of one of ordinary skill in the art in view of the combined teachings of Samain et al. and Ullrich et al. to use any of the recited accessory enzymes in claims 60 and 65 and cell/nucleotide sugar of claim 69 to make the desired sugar nucleotide required for the synthesis of a desired product saccharide. In regard to claims 67 and 68, it would have been obvious to inactivate genes encoding glycosyltransferases that use the produced UDP-GlcNAc for other metabolites or other polysaccharides since such inactivation would facilitate the accumulation of the UDP-GlcNAc for use in the production of penta-N-acetyl-chitopentaose.

Thus, the claims are within the ordinary skill in the art to make and use at the time the invention was made, and was as a whole clearly *prima facie* obvious.

7. Claims 61-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Samain et al. in view of Ullrich et al. as applied to the claims above, and further in view of Bulow et al. (Trends Biotechnol. 1991 Jul;9(7):226-31).

Bulow et al. teach the value of artificial bi-functional enzymes and multienzyme systems obtained by gene fusion in that such enzymes have a great potential in enzyme technology as they facilitate easy purification and favorable enzyme kinetics (see entire publication)

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the above modified method of Samain et al. such that the N-acetylglucosamine 1-phosphate uridyltransferase (heterologous accessory enzyme) and NodC (glycosyltransferase) are expressed as a fusion protein in order to obtain favorable enzyme kinetics such that the nucleotide sugars is generated *in situ* and can be immediately used in the production of the product saccharide. Furthermore, it is within the purview of one of ordinary skill in the art in view of the combined teachings to make fusion proteins using any of the enzymes recited in claims 63 and 64 in the production of the product saccharide.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER